

What is claimed is:

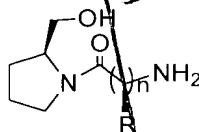
5 1. / A method of treating a subject afflicted with an
infection caused by vancomycin resistant Gram-
positive bacteria in which resistance results from
the conversion of an amide bond to an ester bond in
the cell wall peptide precursors of the bacteria
10 which comprises administering to the subject an
antibacterial amount of vancomycin or a homolog of
vancomycin and an amount of an agent effective to
selectively cleave said ester bond so as to thereby
treat the subject.

15 2. The method of claim 1, wherein the subject is a human
being.

20 3. The method of claim 1, wherein the agent is an
activated nucleophile, and is further characterized
21 by the presence within the agent of an electrophile
and chirality complementary to a bacterial cell wall
depsipeptide.

25 4. The method of claim 1, wherein the agent is
represented by the formula S-Pro-C_n.

30 5. The method of claim 1, wherein the agent has the
structure:



35 wherein n is an integer from 1 to 6 inclusive and R

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is hydrogen or a C₁ to C₆ straight chain or branched alkyl group.

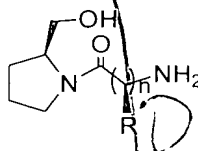
- 5 6. The method of claim 1, where the agent catalytically cleaves said ester bond.
7. The method of claim 1, wherein said ester bond is present in the structure D-Ala-D-Lac.
- 10 8. The method of claim 1, wherein the agent is administered prior to administering vancomycin or the homolog of vancomycin.
- 15 9. The method of claim 8, wherein the agent is administered a sufficient period of time prior to administering vancomycin or the homolog of vancomycin to permit cleavage of said ester bond to be effected.
- 20 10. The method of claim 1, wherein the agent and vancomycin or the homolog of vancomycin are administered simultaneously.
- 25 11. The method of claim 10, wherein the agent is covalently attached to vancomycin or the homolog of vancomycin.
12. The method of claim 1, wherein the bacteria are Van A, Van B, Van D or Van G Gram positive bacteria.
- 30 13. The method of claim 1, wherein the bacteria are Staphylococcus bacteria.

14. The method of claim 12, wherein the bacteria are S. aureus bacteria.
15. The method of claim 1, wherein the bacteria are Enterococcus bacteria.
16. The method of claim 1, wherein the bacteria are Streptococcus bacteria.
17. The method of claim 1, wherein the bacteria are Leuconostoc bacteria.
18. The method of claim 1, wherein the bacteria are Pediococcus bacteria.
19. The method of claim 1, wherein the bacteria are Lactobacillus bacteria.
20. The method of claim 1, wherein the bacteria are Erysipelothrix bacteria.
21. A method of killing vancomycin resistant Van A, Van B, Van D, or Van G Gram-positive bacteria which comprises contacting the bacteria with an agent that selectively cleaves D-Ala-D-Lac cell wall depsipeptides in the bacteria in an amount effective to cleave such depsipeptides and an antibacterial amount of vancomycin or a homolog of vancomycin so as to thereby kill the bacteria.
22. The method of claim 21, wherein the agent is an activated nucleophile, and is further characterized by the presence within the agent of an electrophile

Ex and chirality complementary to a bacterial cell wall
depsipeptide.

23. The method of claim 21, wherein the agent is
5 represented by the formula S-Pro-Cn.

24. The method of claim 21, wherein the agent has the
structure:



15 wherein n is an integer from 1 to 6 inclusive and R
is hydrogen or a C₁ to C₆ straight chain or branched
alkyl group.

Ex 25. The method of claim 21, where the agent catalytically
cleaves said ester bond.

26. The method of claim 21, wherein said ester bond is
present in the structure D-Ala-D-Lac.

27. The method of claim 21, wherein the agent is
25 administered prior to administering vancomycin or the
homolog of vancomycin.

Ex 28. The method of claim 27, wherein the agent is
30 administered a sufficient period of time prior to
administering vancomycin or the homolog of vancomycin
to permit cleavage of said ester bond to be effected.

29. The method of claim 21, wherein the agent and
vancomycin or the homolog of vancomycin are

30. The method of claim 29, wherein the agent is covalently attached to vancomycin or the homolog of vancomycin.

10 32. The method of claim 31, wherein the bacteria are S.
aureus bacteria.

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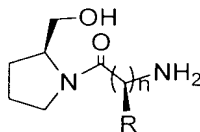
34. The method of claim 21, wherein the bacteria are Streptococcus bacteria.

36. The method of claim 35, wherein the compound comprises the structure D-Ala-D-Lac.

37. The method of claim 35, wherein the compound comprises the structure L-(X-Y) wherein (X-Y) is D-Ala-D-Lac, and wherein L is a detectable label.

45. The method of claim 42, wherein the agent is represented by the formula S-Pro-C_n.

46. The method of claim 42, wherein the agent has the structure:



wherein n is an integer from 1 to 6 inclusive and R is hydrogen or a C₁ to C₆ straight chain or branched alkyl group.

47. The method of claim 42, where the agent catalytically cleaves said ester bond.

48. The method of claim 42, wherein said ester bond is present in the structure D-Ala-D-Lac.

49. The method of claim 42, wherein the agent is administered prior to administering the glycopeptide antibiotic.

50. The method of claim 49, wherein the agent is administered a sufficient period of time prior to administering the glycopeptide antibiotic to permit cleavage of said ester bond to be effected.

51. The method of claim 42, wherein the agent and the glycopeptide antibiotic are administered simultaneously.

52. The method of claim 51, wherein the agent is covalently attached to the glycopeptide antibiotic.
53. The method of claim 42, wherein the bacteria are Staphylococcus bacteria.
54. The method of claim 53, wherein the bacteria are S. aureus bacteria.
55. The method of claim 42, wherein the bacteria are Enterococcus bacteria.
56. The method of claim 42, wherein the bacteria are Streptococcus bacteria.
57. The method of claim 42, wherein the bacteria are Leuconostoc bacteria.
58. The method of claim 42, wherein the bacteria are Pediococcus bacteria.
59. The method of claim 42, wherein the bacteria are Lactobacillus bacteria.
60. The method of claim 42, wherein the bacteria are Erysipelothrix bacteria.
61. A method of killing glycopeptide antibiotic resistant Gram-positive bacteria which comprises contacting the bacteria with an agent that selectively cleaves D-Ala-D-Lac cell wall depsipeptides in the bacteria in an amount effective to cleave such depsipeptides and

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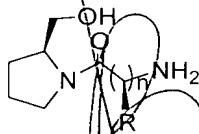
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an antibacterial amount of the glycopeptide antibiotic so as to thereby kill the bacteria.

62. The method of claim 61, wherein the agent is an activated nucleophile, and is further characterized by the presence within the agent of an electrophile and chirality complementary to a bacterial cell wall depsipeptide.

63. The method of claim 61, wherein the agent is represented by the formula S-Pro-Cn.

64. The method of claim 61, wherein the agent has the structure:



wherein n is an integer from 1 to 6 inclusive and R is hydrogen or a C₁ to C₆ straight chain or branched alkyl group.

65. The method of claim 61, where the agent catalytically cleaves said ester bond.

66. The method of claim 61, wherein said ester bond is present in the structure D-Ala-D-Lac.

67. The method of claim 61, wherein the agent is administered prior to administering the glycopeptide antibiotic.

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